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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
PRIEBE, SCOTT DAVID

ART UNIT	PAPER NUMBER
1632	9

DATE MAILED: 11/05/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/922,227	Ruoslahti et al.
Examiner	**Art Unit**
Scott D. Priebe, Ph.D.	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) [X] Responsive to communication(s) filed on *Aug 2, 2001*.

2a) [X] This action is **FINAL.** 2b) [ ] This action is non-final.

3) [ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) [X] Claim(s) *1-6* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) [ ] Claim(s) _____ is/are allowed.

6) [X] Claim(s) *1-6* is/are rejected.

7) [ ] Claim(s) _____ is/are objected to.

8) [ ] Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) [X] The specification is objected to by the Examiner.

10) [ ] The drawing(s) filed on _____ is/are a) [ ] accepted or b) [ ] objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) [ ] The proposed drawing correction filed on _____ is: a) [ ] approved b) [ ] disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) [ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) [ ] All b) [ ] Some* c) [ ] None of:

1. [ ] Certified copies of the priority documents have been received.
2. [ ] Certified copies of the priority documents have been received in Application No. _____.
3. [ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) [ ] The translation of the foreign language provisional application has been received.

15) [X] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) [X] Notice of References Cited (PTO-892)	4) [ ] Interview Summary (PTO-413) Paper No(s).
2) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) [ ] Notice of Informal Patent Application (PTO-152)
3) [X] Information Disclosure Statement(s) (PTO-1449) Paper No(s). 4	6) [ ] Other:

DETAILED ACTION

Specification

The disclosure is objected to because of the following informalities:

In the first sentence of the specification, the status of the parent applications, e.g. whether abandoned or patented, should be updated. If patented, the US patent number should be indicated.

The specification at page 6, line 31, to page 7, line 1 defines "peptide" in a manner repugnant to the art. The term "peptide" has a definite art recognized meaning, this meaning does not include "peptoids" and "peptidomimetics". At page 18, lines 19-26, "organ" is defined so as to include tissue, cells, and tumors. The term "organ" has an art recognized meaning that does not include tissue, cells, and tumors. Although Applicants are entitled to be their own lexicographer, this does not extend to redefining terms that have specific art recognized meanings.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 and 6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods using a library of diverse molecules, each

molecule conjugated to a tag to provide recovery means and/or a polynucleotide tag that can be amplified by polymerase chain reaction to provide identification means, does not reasonably provide enablement for any other embodiment of the claimed invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are broadly drawn to a method of screening or panning a library of any unspecified organic molecules, which molecules may each be attached to a tag, taking a sample of a desired organ or tissue, and identifying a library member. It is noted that "molecule" is defined in the specification at page 6, lines 24-25, as an organic molecule. The specification teaches but a single use for a plurality of different library members that share the property of homing to a particular tissue, to then identify the library members that home to the target tissue so that a homing molecule can be produced and used as a targeting ligand for a variety of applications. Consequently, only the identified end products have utility and the claims must be enabled for the further step of identifying individual library members in the plurality obtained by the method.

The prior art is totally silent on the claimed methodology. The only related prior art involves phage display libraries of peptides. Likewise, all of the working examples provided in the specification are directed at screening libraries of display phage. Unlike other libraries encompassed by the claims, peptide libraries displayed on bacteriophage comprise both a means for recovery, the phage, and identification, the recombinant phage genome encoding a coat fusion

protein comprising the peptide library member. The specification discloses several means, i.e. tags, for recovery of a library member, a physical support such as a microbead or phage, and biotin. The specification teaches but a single type of tag for identification of an individual library member, a nucleic acid.

The specification lists only three specific types of libraries of organic molecules, nucleic acid, peptides and peptide mimics; the term "drug" imparts no structural characteristics of the "organic molecules". In contrast, the claim reads on any conceivable organic compound library as well as those yet to be conceived. The specification does not teach how to make any library of organic molecules or any individual organic molecule which would be in such a library, although a variety of such libraries were known in the art. Instead, the specification relies in general on that which was well known in the art. It is accepted that the methods for making nucleic acid and peptide libraries in general and certain peptide mimic libraries were known to the pertinent artisans, however, this does not extend to any and all possible libraries of organic compounds in general. Also, the specification does not suggest which of all possible organic molecule libraries other than polynucleotides, polypeptides, and peptide mimics would be likely to yield at least one compound that would home to a given tissue or organ, and the deficiency is not remedied by what was well known in the prior art. Since the claimed invention borders on a pioneering invention, it cannot have been routine in the art to make and test various types of library to determine the identity of types of libraries that would provide at least one member that would

home to a given target tissue, and one certainly could not predict the identity of such library types in general.

The specification fails to teach how any and all individual organic molecules from the library would be identified in a tissue of organ sample to complete the method or any and all methods of identification encompassed by the breadth of the claims. Rather, the specification simply suggests that those artisans familiar with the particular organic compound would know how to obtain a crude preparation in which the organic molecules are enriched and would be able to identify the individual compounds, or teaches that the individual compounds could be tagged. However, the specification does not teach how any and all organic compounds could be tagged or which tags could be attached to each particular class of organic molecules which might make up the library. One skilled in the art would know how to attach tags to members of some types of library, but the specification describes only polynucleotides, polypeptides and poly-peptide mimics, which it is noted are all heteropolymeric compounds.

The specification (pages 8-10) adequately describes only one method for identifying the individual organic compounds, which relies on tagging the organic molecules with an oligonucleotide with a sequence specific to the individual molecule. The specification also mentions in passing that mass spectroscopy and gas chromatography could be used, especially for "drug" libraries, but fails to elaborate on how this would be done, especially since the samples, regardless of initial processing to enrich for library compounds, would be a complex mixture. It is unclear whether or not any given organic compound could be tagged, or tagged so that the tag

would not interfere with binding to a "receptor" present in the tissue or organ. In the case of heteropolymer libraries, the latter would not be expected to be a problem, but could be a significant problem with small organic molecules.

In order to identify the individual molecule, each distinct species in the library would have to be tagged with a specific tag that identified the organic compound to which it is attached. The only specific tag disclosed in the specification is a nucleic acid tag, which could be enzymatically amplified and then ultimately sequenced. This tagging system places constraints on the type of nucleic acid that could be used, namely that it can serve as a template for PCR. However, the specification fails to identify which of the myriad synthetic nucleic acids can serve as such a template in addition to natural nucleic acids. However, it is unclear whether natural nucleic acids could survive the claimed assay. Hicke et al. discloses a method of administering a nucleic acid aptamer to a subject. The method employed by Hicke et al. involved administering identical aptamer molecules to the subject, not a mixture of different aptamers. The survival of the aptamer was inferred by the observation of its biological activity, it was not isolated from the subject. Furthermore, Hicke et al. used PEGylated aptamers to protect them from nucleases, even so the aptamer was degraded with a half-life of 18 min., which was "significantly longer than that of unmodified ssDNA aptamers" (see page 2691, col. 2). PEGylation is not taught in the instant specification and it is unclear whether such PEGylated DNA could subsequently serve as a template for PCR in order to identify an aptamer or any other organic molecule to which a DNA tag might be conjugated. Stephens et al., US 5,688,935, discloses that RNA SELEX libraries can

be panned *in vivo* and individual molecules identified and obtained. The results indicate that tags consisting of RNA would not be degraded *in vivo* during a 15 minute exposure to the extent that the tag would be unidentifiable. However, with respect to identifier tags, if limited to polynucleotides that can amplified by PCR, one skilled in the art would not need to engage in undue experimentation.

Therefore, in light of the generalized description of the method with little specific information for practicing the myriad possible embodiments of the invention, other than organic molecules that are peptides and poly-peptide mimics; the lack of teaching in the prior art concerning this methodology and the pioneering nature of the invention; the lack of relevant working examples; and the limited disclosure of methods of identification of individual compounds in the samples, i.e. polynucleotide tags, it would require excessive experimentation involving inventive effort on the part of the skilled artisan to practice any single embodiment of the claimed invention, and even more so to practice the invention throughout its claimed scope. Such experimentation is undue.

A patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion. Tossing out the germ of an idea does not constitute an enabling disclosure. While every aspect of a generic claim need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable the skilled artisan to understand and carry out the invention. It is true that a specification need not disclose what is well known in the art. However, that general, oft-repeated statement is merely a rule of

supplementation, not a substitute for a basic enabling disclosure. The rule that a specification need not disclose that which is well known in the art simply means that omission of minor details does not cause a specification to fail the enablement requirement, and is not a substitute for an enabling disclosure. However, if there is no disclosure of starting materials and of conditions under which the process can be carried out, undue experimentation is required. Failure to provide such teachings can not be rectified by asserting that the disclosure of the missing necessary information was well known in the prior art. See *Genentech Inc. v. Novo Nordisk A/S*, 42 USPQ2d 101, 1005 (CA FC, 1997). The only embodiments for which the specification meets the burden imposed under 35 USC 112, 1st para. have been indicated above.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is incomplete, the final method step does not clearly relate back to the preamble in that "identifying" is not "obtaining"; it is suggested that "obtaining" in the preamble be replaced by --identifying--.

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the

invention. In claim 5, it is unclear whether "said molecule" applies only to the molecule identified or to all of the "diverse molecules" of the library.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claims 1, 2 and 6 are rejected under 35 U.S.C. 102(e) as being anticipated by Stephens et al. US 5,688,935.

Stephens et al. disclose a method for screening a library of diverse, non-naturally occurring, tagged nucleic acid molecules by panning against intact tissue samples *in vitro* or against tissue and organs *in vivo* (at least RNA), such as brain, kidney, tumor tissue and arterial walls. The method allows identification and isolation of individual library members that "home" to specific tissues. The PCR priming sequences at the ends of the library members constitute shared tags and the intervening sequence is both reactant and identifying tag. The reference also

discloses tissue samples comprising members of such a library. The library was introduced into a non-human mammal by intrvenous injection (See col. 3, line 19 to col. 4, line 11 (overview); col. 5, line 6 to col. 6, line 16; col. 23, line 65 to col. 28, line 25).

Double Patenting

Applicant is advised that should claim 4 be found allowable, claim 5 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim 5 depends from claim 4 which recites that the library is a phage display library. In so much as phage display libraries are peptide or protein libraries, i.e. the displayed molecules are peptides, and peptide libraries as a genus include phage display libraries, recitation in claim 5 that the molecule is a peptide does not further limit the scope of claim 4.

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 4 is rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 1 of prior U.S. Patent No. 5,622,699. This is a double patenting rejection.

Although claim 4 is not identical to claim 1 of the '699 patent, "organ" is defined in the instant specification to embrace tissues and cells, such that the scope of the conflicting claims is identical.

Claims 1-3, 5 and 6 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 5,622,699. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims fully embrace (and are anticipated by) the claimed subject matter of the '699 patent.

Claims 1-6 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-21 of U.S. Patent No. 6,068,829. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims fully embrace (and are anticipated by) the claimed subject matter of the '829 patent.

Claims 1-6 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 6,296,832. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claimed library fractions of the '832 patent are recited as being made by a process which is embraced by the instant claims.

Claims 1-6 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-19 of U.S. Patent No. 6,306,365. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claims fully embrace (and are anticipated by) the claimed subject matter of the '365 patent. In light of the specification of the '365 patent, "diverse molecules" is explicitly disclosed as embracing peptides.

Certain papers related to this application may be submitted to Art Unit 1632 by facsimile transmission. The FAX numbers are (703) 308-4242 or (703) 305-3014 for any type of communication. In addition, FAX numbers for a computer server system using RightFAX are also available for communications before final rejection, (703) 872-9306, and for communications after final rejection, (703) 872-9307, which will generate a return receipt. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (703) 308-7310. The examiner can normally be reached on Monday through Friday from 8 AM to 4 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051.

Any inquiry concerning administrative, procedural or formal matters relating to this application should be directed to Patent Analyst Patsy Zimmerman whose telephone number is (703) 308-8338. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Scott D Priebe

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